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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/580,660	03/08/2007	Robert Hofmeister	DEBE:066US/10605466	1727

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EXAMINER	
NATARAJAN, MEERA	
ART UNIT	PAPER NUMBER
1643	

MAIL DATE	DELIVERY MODE
04/24/2009	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/580,660	HOFMEISTER ET AL.	
	Examiner	Art Unit	
	MEERA NATARAJAN	1643	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *29 December 2008*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *26 and 30-50* is/are pending in the application.

4a) Of the above claim(s) *30-50* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *26* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. Applicant's amendments in the reply filed on 12/29/2008 is acknowledged and entered into the record.

2. According, Claims 1-25, 27-29 have been cancelled by Applicant. Claims 30-50 have been withdrawn as being drawn to non-elected inventions.

3. Claim 26 is pending and will be examined on the merits.

Claim Rejections Maintained - 35 USC § 112

4. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

5. The rejection of Claim 26 under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement is maintained for the reasons of record. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

6. Claim 26 is drawn to polypeptides having a sequence that is at least 70% homologous to any of SEQ ID NOs: 1-6.

7. As stated in the previous office action, the Applicant has not provided adequate written description of any identifying characteristics, physical or chemical properties, or a correlation between function and structure of the claimed 70% homologous to SEQ ID NOs 1-6 polypeptides. Applicants argue that "the specification discloses methods for

carrying out sequence alignments which can be used to identify bispecific constructs which are at least 70% homologous to the CD3 and CD19 binding construct depicted in SEQ ID NOs: 1-6". This argument has been carefully considered but not found persuasive. Applicants have not provided specific detail on which amino acids are necessary for binding to CD19. Although the specification provides screening methods for altering amino acids of the claimed polypeptide, one of ordinary skill in the art, based on the guidance provided in the specification, would not know which amino acids are essentially for antigen binding and which amino acids could be altered. Therefore, the specification does not provide for sufficient written description to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, Applicant had possession of a reasonable number of sequences which are 70% homologous to SEQ ID NO:1, which retain the function of binding to CD19. The specification only provides adequate written description for 100% homology with SEQ ID NOs: 1-6. The rejection of record is maintained.

8. The rejection of Claim 26 under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a composition comprising a polypeptide having a sequence that is 100% identical to SEQ ID NOs:1-6, does not reasonably provide enablement for a composition comprising a polypeptide having a sequence that is at least 70% homologous to SEQ ID NOs: 1-6 is maintained for the reasons of record.

9. Applicants did not provide arguments in the response filed 12/29/2008 to support withdrawal of the enablement rejection of record. Therefore the rejection is maintained for the reasons of record.

Claim Rejections Maintained - 35 USC § 102

10. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

11. The rejection of Claim 26 under 35 U.S.C. 102(b) as being anticipated by Dorken et al. (US Patent 7112324) is maintained for the reasons of record.

12. The claim is drawn to a composition comprising a polypeptide comprising at least two antigen binding sites, wherein said at least two antigen binding sites are located on a single polypeptide chain and wherein one antigen binding site specifically binds the human CD3 antigen and the other binding site specifically binds to the human CD19 antigen comprising SEQ ID NO:1, said polypeptide having both monomeric and multimeric form and wherein the multimeric form of said polypeptide constitutes no more than 5% of the total weight of the combined monomeric and multimeric forms of said polypeptide.

13. Dorken et al. teach “single-chain multifunctional polypeptides comprising at least two binding sites specific for the CD19 and CD3 antigen” (see Abstract). Dorken et al. teach a polypeptide with binding sites specifically to human CD19 antigen and wherein said polypeptide has a sequence that is 100% homologous to SEQ ID NO: 1. The limitation recited in the claims wherein said polypeptide constitutes no more than 5% of the total weight of the combined monomeric and multimeric forms of said polypeptide

are described in the specification to be achieved through methods of "enrichment" involving resolution ion-exchange HPLC, high resolution size exclusion chromatography, gel purification, etc (see specification p.12-13). Dorken et al. disclose methods of purification involving "imidazole gradient", gel filtration (see Fig. 14 legend), cation exchange chromatography (see fig. 12 legend), gel electrophoresis (see Fig. 11 legend), etc. Based on the teachings provided in the instant specification, the methods of purification taught by Dorken et al. would result in a polypeptide constituting no more than 5% of the total weight of the combined monomeric and multimeric forms of said polypeptide.

14. Applicants argue the purification method described in Example 6 of Dorken et al. would dissociate all the multimeric proteins into monomeric proteins and therefore Dorken et al. does not anticipate the claimed polypeptide. Applicants argue that the claimed polypeptide with the ratio of monomeric to multimeric proteins is obtained by the inventive processes of the present invention and only through these processes are the skilled artisan able to separate the monomeric and multimeric form of the bispecific antibody constructs and to obtain the mixture with the claimed ratio. These arguments have been carefully considered but not found persuasive.

15. Dorken et al. disclose several different methods of purifying the bispecific antibody construct. The instant claim is drafted in the product-by-process format. As stated in the previous office action and restated above, the process described in the specification to obtained the desired ratio of monomeric to multimeric is achieved through methods of "enrichment" involving resolution ion-exchange HPLC, high

resolution size exclusion chromatography, gel purification, etc (see specification p.12-13). Although, the references do not describe the production of the molecule using the methods identical to that is recited in claim, Dorken discloses the polypeptides of the present invention can be purified according to standard procedures of the art including column chromatography as described in the instant specification. The rejection of record is therefore maintained.

Conclusion

10. Claim 26 is rejected.

11. No Claim is allowed.

12. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

13. Any inquiry concerning this communication or earlier communications from the examiner should be directed to MEERA NATARAJAN whose telephone number is

(571)270-3058. The examiner can normally be reached on Monday-Thursday, 9:30AM-7:00PM, ALT. Friday. EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Larry Helms can be reached on 571-272-0832. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

MN

/Larry R. Helms/
Supervisory Patent Examiner, Art Unit 1643